Hereditary Osteo-Onycho-Dysplasia—The Nail-Patella Syndrome

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HEREDITARY osteo-onycho-dysplasia or HOOD (nail-patella syndrome) consists of a group of hereditary anomalies primarily affecting the nails, elbows, pelvis and knees. Although considered rare, the condition may be more common than is realized. Patients are frequently treated for a single feature without recognition of the entire syndrome.[6] Most patients are asymptomatic, the anomalies being found after medical advice was sought for unrelated conditions[2] and a history and examination of the patient's family reveals others affected with the syndrome.

The recent examination of two patients with HOOD and their families prompted this report, with attention to salient features that may lead to early diagnosis. A further item of the report is the relatively recent awareness of nephropathy in this syndrome.

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Features of HOOD

Nails

Nail dystrophy is the commonest feature of HOOD, with an incidence of 93[4] and 98[2] percent reported in large series. In any case in which dystrophy of nails occurred, thumbnails were always affected, with other nails less frequently and less severely involved. The changes may include the toenails.

The spectrum of abnormalities may vary from slight longitudinal ridging to complete absence of a nail. Usual changes consist of hypoplasia, thinning and longitudinal ridging. In many instances nails are split in two by a longitudinal cleft and the lunules are poorly formed.[2] Abnormalities are symmetrical and persist throughout life. Nail-patella syndrome may be diagnosed at birth from nail changes.[14]

Knees

Knee changes occur in approximately 90 percent of cases.[2,4] The vast majority of patients have patellar hypoplasia, although absence, subluxation and dislocation are also prominent features. The shape of the hypoplastic patella may be ovoid, triangular or irregular.

The medial femoral condyle is frequently large and the lateral small. The tibiae may rotate laterally. Frequently the patellar tendons are lax.

The patella may be subluxated or completely dislocated. Recurrent dislocation may be a serious problem and it appears to be the major reason patients seek medical advice for the nail-patella syndrome. The tendency for the patella to dislocate laterally may produce a considerable walking impediment, particularly walking downstairs. Early osteoarthritis frequently occurs. Affected infants may be slow to walk and have an abnormal gait.

Elbows

Elbows are involved about as commonly as the knees—that is, in 90 percent of patients.[2,4]

The essential feature is hypoplasia of the lateral side of the joint. The carrying angle is frequently increased and there may be an enlargement of the medial epicondyle. Hypoplasia involves the radial head particularly, but may involve the capitellum and lateral epicondyle also.

The radial head may articulate normally with the capitellum but may be subluxated or completely dislocated. Changes, unlike those of nail dystrophy, may be asymmetrical. Dislocation is nearly always posterolateral and if it is complete the radial head is small and rounded and the neck elongated and narrowed. Mild to moderately severe impairment of extension, pronation and supination of the forearm may be present.[14]

Pelvis

"Iliac horns" are the pathognomonic feature of this syndrome, but they are not always present. Since these harmless functionless bony projections are obscured they are frequently overlooked, and this is reflected in the low incidence of this finding in some series. Careful evaluation has revealed iliac horns in 87 percent[2] of cases of HOOD.

Iliac horns arise from the posterior aspects of the ilii. Each may have an epiphysis-like cap or secondary center of ossification at its tip. They vary from a faint sclerotic line to 4 cm in length. They frequently are easily palpable and are sometimes visible. They are invariably bilateral and usually symmetrical. They are present as early as six months of age.

Flaring of the iliac crests has been reported[4] with the pelvis assuming a winged appearance likened by Lacroux[13] to elephant ears.

Associated Anomalies

Nephropathic Changes

Renal dysplasia appears to be an infrequent but potentially fatal component of the nail-patella syndrome. Hawkins and Smith[8] are credited with the first reports of kidney dysfunction in HOOD when they reported a family in which the propositus had died and changes typical of chronic glomerulonephritis noted at autopsy. The grandmother of the propositus had died of "dropsy" and his uncle and brother had albuminuria.

"Chronic glomerulonephritis" was reported on autopsy of another patient with HOOD who died at age 26 of nephritis.[1] Jameson, Lawler and Renwick[9] also report cases of "Bright's disease," "chronic nephritis," "chronic glomerulonephritis" and "chronic albuminuria." A 20-year-old woman with HOOD and a nephrosis-like clinical course, had focal glomerulonecrosis and diffuse tubular degeneration of the kidneys.[7] Muth[15] studied another patient who had a complete renal evaluation including percutaneous renal biopsy, because of persistent proteinuria. Eighty percent of the glomeruli in the biopsy specimen had mainly minor changes consisting for the most part of small areas of endothelial and epithelial cell proliferation.

Carbonara and Alpert in 1964[2] reviewed cases of HOOD in the American literature since 1948. They found proteinuria present in 42 percent of cases in which urinalysis was mentioned.

Iris Pigmentation

A defect in the iris reported in patients with HOOD consists of an outer zone of pale pigment and an inner zone of dark coloration arranged like a cloverleaf[3,11] ("Lester's sign"). Cosack[3] reported this anomaly in family members unaffected by HOOD, and this is related to another gene, which may be linked with other sporadic anomalies to the nail patella syndrome.[2]

Infrequent Anomalies

Small incidences of other defects have been reported, including mental deficiency, postural changes, and wrist and shoulder abnormalities, which appear to be coincidental.

Metabolic studies have revealed excessive urinary excretion of acid mucopolysaccharides. This change is not specific and has been seen in other generalized skeletal disorders.[2,12]

Genetic Studies

HOOD is transmitted as a non-sex linked dominant character. All affected persons have an affected parent. Complete transmission of the trait has been reported through six successive generations.[5] Since genes are paired, one would expect a parent with this dominant trait to pass it on to half his offspring, and large studies bear this out.[5]

The gene expresses itself variably, the nail changes almost always being present with various combinations of elbow, pelvic and knee involvement.

Lawler, Renwick and coworkers[10,16] have shown that the responsible gene lies on the same chromosome as the ABO blood group locus. In any given family the gene for the syndrome will be transmitted in association with only one of the genes of A, B or O.

Case Report and Family Survey

CASE 1.—A 15-year-old girl was admitted to St. Joseph Hospital on 19 September 1966 because of pain in the right lower quadrant of the abdomen. In June 1966, this patient had been seen because of a urinary tract infection and she received uroseptic drugs for one month.

Because of the abdominal pain, abdominal films were obtained. They demonstrated well developed iliac horns (Figure 1). The patient also had the remainder of the classic tetrad—dysplastic nails, radial head subluxation (Figure 2), and rudimentary patellae (Figure 3).

Results of routine laboratory tests, an intravenous pyelogram and a lower gastrointestinal series were all within limits of normal. The patient's symptoms subsided and she was discharged.

This patient is the only one of four siblings with the syndrome. The propositus mother has involvement of nails, knees and elbows; and she is the only one of three siblings with any involvement. The maternal grandmother has the same involvement and of three siblings is the only one affected.

The next two preceding generations affected involved the maternal great grandfather and great-great grandfather, and it was known that in them the nails and the knees were affected.

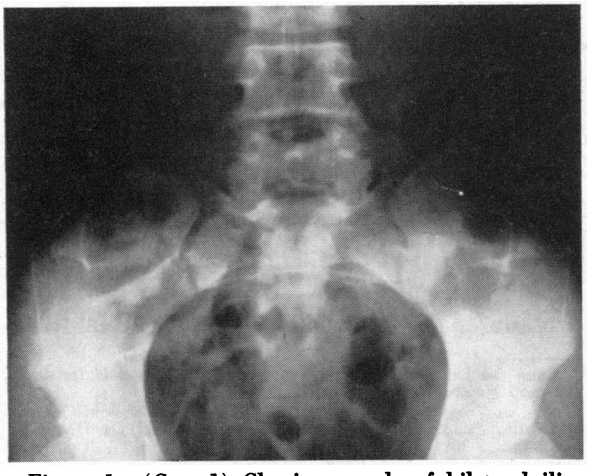

Figure 1.—(Case 1) Classic example of bilateral iliac horns seen on abdominal survey before barium enema study.

CASE 2.—A 16-year-old girl was first admitted to the Orthopedic Service of St. Joseph Hospital 1 July 1966 on complaint of a knobby appearance of the elbows. Physical examination revealed bilateral radial head disclocation, with minus 10 degrees of supination in both elbows (Figure 4). The patient was also known to have recurrent dislocation of the patella. The right radial head was removed, with good results, and correction of the left elbow was planned for a later date. Other pertinent findings were fissuring of all the nails and hypoplasia of the patellae. Iliac horns were not demonstrated. This patient's mother, an aunt and an uncle have involvement of nails, knees and

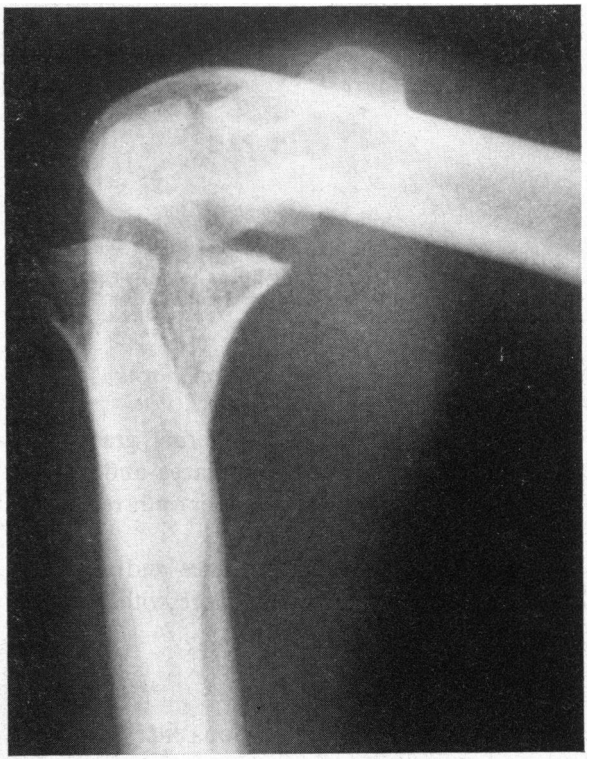

Figure 2.—(Case 1) Posterior subluxation of radial head.

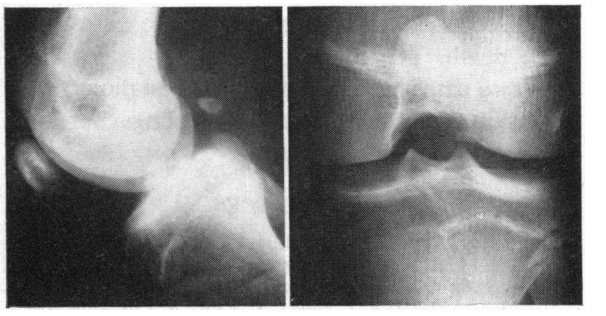

Figure 3.—(Case 1) Hypoplastic patella.

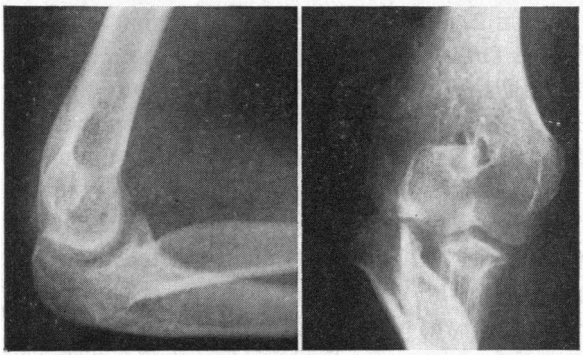

Figure 4.— (Case 2) Dislocation of radial head with greater deformity than in Case 1.

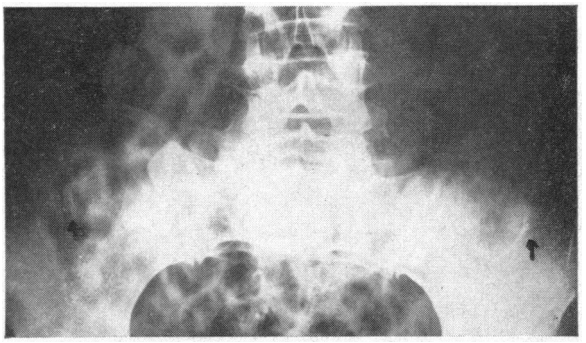

Figure 5.—Rudimentary iliac horns (arrows) in mother of patient in Case 2. (Propositus did not exhibit this manifestation.)

elbows. The mother had iliac horns as well (Figure 5).

Inquiry elicited that the maternal grandfather had involvement of the nails, knees and elbows. He had three sisters and a brother with reportedly no involvement.

Results of routine blood studies and urinalysis of the patient and her mother were within normal limits.

Summary

The principal manifestations of hereditary osteo-onycho-dysplasia consist of nail dystrophy, elbow dysplasia, hypoplasia or complete absence of patella, and the presence of iliac horns. Nephropathic concomitants, present in some cases, may cause death.

In two cases here reported, manifestations of the condition were not present in siblings but were known in some progenitors.

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Intrauterine Transfusion of Twins

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BEGINNING WITH the first case report of a successful fetal transfusion by Liley,[10] numerous articles have appeared in the literature describing modifications, complications and results with this procedure. The following is a report of fetal trans-

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